01/13/97 THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

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Robert M. LORENCE ET AL.

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Serial No.: 08/260,536

Group Aft Unito 18130

A CL

Filed: June 16, 1994

Examiner: L. Scheiner

For:

1477 U.S. PTO

METHODS FOR TREATING AND DETECTING CANCER USING VIRUSES

DECLARATION UNDER 37 CFR § 1.132 OF DR. MARK PEEPLES

- I, Mark Peeples, declare and state as follows:
- 1. I reside at 1906 South Maple Avenue, Berwyn, Illinois 60402.
- 2. I am presently a Professor at Rush Medical College, Chicago, Illinois 60402. Currently, I am a visiting scientist at the Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland.
- 3. In 1974, I received a Bachelor of Arts in Biology and German from Heidelberg College, Tiffin, Ohio. In 1978, I received a Doctor of Philosophy in Immunology and Microbiology from Wayne State University, Detroit, Michigan. In 1978, I began my postdoctoral studies on Newcastle disease virus ("NDV") at the University of Massachusetts Medical School in Worcester, Massachusetts. I have worked with NDV for the past 18 years, and continue to do so.
- 4. My complete academic background and professional experience are set forth in my curriculum vitae, a copy of which is attached as Exhibit A.
- 5. I have conducted considerable research relating to Newcastle Disease Virus as reflected in the many publications I have written in this area.
- 6. I have read and considered the specifications corresponding to U.S. Application Serial Nos. 08/055,519 and 08/260,536, filed on April 30, 1993 and June 16, 1994, respectively ("patent applications"). These applications describe, among other things, methods of treating and detecting cancer in mammals using Paramyxoviruses, such as Newcastle Disease Virus ("NDV").

- 7. It is my opinion, as an expert in NDV, that the above-mentioned patent applications necessarily convey to one of skill in the art the concept of treating cancer in a mammal with a "mesogenic" NDV. My opinion is based on the following paragraphs:
- 8. NDV is categorized into three distinct classes according to its effects on chickens and chicken embryos. "Low virulence" strains are referred to as lentogenic and take 90 to 150 hours to kill chicken embryos at the minimum lethal dose (MLD); "moderate virulence" strains are referred to as mesogenic and take 60 to 90 hours to kill chicken embryos at the MLD; "high virulence" strains are referred to as velogenic and take 40 to 60 hours to kill chicken embryos at the MLD. See, e.g., Hanson and Brandly, Science, 122:156-157, 1955 and Dardiri et al., Am. J. Vet. Res., 918-920, 1961.
- 9. The patent applications describe NDV as useful to treat and detect cancer in mammals. Since the entire NDV class is comprised of lentogenic, mesogenic, and velogenic, the disclosure in the patent application necessarily conveys to one of skill in the art that each of these three categories is inherently included. On this basis alone, I conclude that the patent applications clearly communicate to the skilled worker that mesogenic NDV is employable for treating cancer in mammals.
 - 10. This is particularly strongly the case for mesogenic NDV.
- (a) The patent applications specifically exemplify a mesogenic NDV strain to treat cancer. Example 3, page 18 of 08/055,519, and Example 3, page 27 of 08/260,536, describe tumor regression after administration of NDV strain M (Mass-MK107). NDV strain M (Mass-MK107) is well known to be a mesogenic type of Newcastle Disease Virus. See, e.g., Schloer and Hanson, *J. Virol.*, 2:40-47, 1968. Consequently, it would have been necessarily understood by one of skill in the art that mesogenic strains are specifically included in the methods of treatment described in the patent applications.
- (b) Although the specific term "mesogenic" is not expressly recited in the patent applications, a synonym for it is mentioned. In the legend to Figure 5 on page 6 of 08/055,519 and page 6 of 08/260,536 it is stated that "Figure 5 illustrates the effectiveness of a strain (M, Mass MK107) of relatively moderate virulence with that of a strain of high virulence (73-T) in causing tumor regression." (Emphasis added.) As discussed above, "mesogenic" is used to identify NDV viruses possessing "moderate virulence" on a relative scale. In Dardiri et al., *supra*, it is stated: "The variations in

virulence are described by the terms 'lentogenic,' low virulence; 'mesogenic,' moderate virulence; and 'velogenic,' high virulence." The latter two definitions are the exact phrases used in the patent applications.

As can be seen, mention of the mesogenic strain M and use of the synonym "moderate virulence" particularly clearly communicate the concept of using mesogenic NDV to treat cancer.

11. In sum, it is my conclusion upon reading the patent applications that the concept of treating cancer in a mammal employing a "mesogenic" strain of NDV is at least inherently, if not explicitly, described.

Further declarant says that all statements made herein are of his own knowledge true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated:

Mark Peeples

CURRICULUM VITAE

MARK EDWARD PEEPLES, Ph.D.

BUSINESS	Department of Immunology/Microbiology	
ADDRESS:	Rush-Presbyterian-St. Luke's Medical Center	
	1653 West Congress Parkway	•
	Chicago, Illinois 60612	
	Telephone: (312) 942-8736	
	FAX: (312) 942-2808	
номе	1906 South Maple Avenue	
ADDRESS:	Berwyn, Illinois 60402	
	Telephone: (708) 795-1236	
PERSONAL:	Born: September 26, 1952	
	Married, no children	
	Social Security Number: 197-42-5399	
	Passport Number: 070832663	
PROFESSIONAL	Postdoctoral Fellow	1978-8
POSITIONS:	Instructor	1980-8
	Department of Molecular Genetics and Microbiology	
	University of Massachusetts Medical School	
	Worcester, Massachusetts	
	Assistant Professor	1983-8
	Associate Professor	1988-9
	Professor	1993-
	Department of Immunology/Microbiology,	
	Rush Medical College and	
	Division of Immunology, Graduate College	
	Rush University, Chicago, Illinois	
	Member	1986-
	Division of Cell Biology, Graduate College	
	Rush University, Chicago, Illinois	
	Head	1989-
	Section of Virology	
	Department of Immunology/Microbiology	
	Rush Medical College Rush University	

Chicago, Illinois

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	Associate Scientist		1989-92
	Scientist		1993-
	Rush-Presbyterian-St. Luke's Medical Center Staff		270
	Associate Chairman	1990-	
	Department of Immunology/Microbiology		
	Rush Medical College, Rush University		
	Chicago, Illinois		
	Sabbatical		1995-96
	Laboratory of Infectious Diseases		
	National Institute of Allergy and Infectious Diseases		
	National Institutes of Health, Bethesda, Maryland		
	Working with Peter Collins		
EDUCATION:	Bachelor of Science		1970-74
	Biology and German		
	Heidelberg College, Tiffin, Ohio		
	Doctor of Philosophy		1974-78
	Immunology and Microbiology		
	Dissertation with Dr. Seymour Levine		
	Wayne State University School of Medicine, Detroit, Michigan		
	Postdoctoral Studies		1978-83
	with Dr. Michael A. Bratt, Department of Molecular Genetics		
	and Microbiology, University of Massachusetts		
	Medical School, Worcester, Massachusetts	•	
HONORS:	DeVlieg Fellowship		1975-76
	NIH Postdoctoral Fellowship		1978-81
	NIH Research Career Development Award		1988-93
	Certificate of Recognition, Rush Sigma Xi Club		1991
	Listed in "Marquis Who's Who in Science and Engineering"		1993,
TEACHING:	Course Director		
	Microbiology Concepts, Medical College		1985-96
	Animal Virology, Graduate College	1984,	86,91,95
	Basic Microbiology, Graduate College		1987
	Loyola Medical School: Virology Unit		1990
	Virus Mimicry, Graduate College		1993
	Lecturer		
	Microbiology Concepts, Medical College		1984-
	(including lab section and facilitating small group problem solv	ing)	

	Animal Virology Graduata Callaga	1004
	Animal Virology, Graduate College Basic Microbiology, Graduate College	1984-
	Host Defense, Graduate College	1987
	Molecular Cell Biology, Graduate College	1987,90
		1988-
	Microbiology, Medical College Alternative Curriculum Medical Technology Virology, College of Health	1988-
	Sciences	1986-94
•	Virology Course, Department of Micrology and	
	Immunology, Northwestern Medical School	1991
	Virology Course, Department of Microbiology and	
	Immunology, Loyola Medical School	1992
	Molecular Biology, Graduate College	1994-
ORGANIZING:	Virology Research/Journal Club	1983-95
	Immunology/Microbiology-Infectious Disease	
	Joint Conferences	1989-95
	Immunology/Microbiology Seminar Series	1990-92
	Molecular Biology Working Group	1991-
	American Cancer Society, Institutional Research	
	Grant; Application and Administration	1991-95
	••• • • • • • • • • • • • • • • • • •	
COMMITTEE	University	4007.00
MEMBERSHIP:	University Committee on Research	1987-90
	University Research Week Committee	1989-
	Search Committee for Chairperson of the	1000 00
	Department of Religion and Health Liaison Committee on Medical Education,	1989-90
•	Research Subcommittee	1000
		1990
	Scientific Misconduct Investigation Committee Student Affairs Committee	1994-
	Student Attairs Committee	1994-95
	Medical College	1000.00
	Medical College Faculty Council	1989-93
	Research Task Force	1991
	Search Committee for Chairperson of the	1000.01
	Department of Preventive Medicine	1990-91
	Search Committee for Chairperson of the	1000.00
	Department of Internal Medicine	1992-93
	Search Committee, Dean of the Medical College	1994
	Head, Pharmacology/Immunology Faculty Search Committee	1994
	Graduate College	4000 0 .
	Graduate College Council	1989-94
	Search Committee for Head of the Division	1000
	of Cell Biology	1989

	Chairman, Graduate College Curriculum Committee	1991-94
	Department	
	Faculty Search Committee, Chairman	1984,88,91-92
	Graduate Advisory Committee	1984-87
	Department Advisory Committee	1985-
	Faculty Search Committee	1994
	Student Dissertation Advisory Committees (23)	1983-
e	as Chairman (5)	
•	as Advisor (7)	•
	as Co-Advisor (1)	
	as Member (5)	
	in another department (4)	
	in another institution (4)	
	National, State, Local	
	Associate Editor, Virology	1987-
	Special NIH Study Section: Programs of	
	Excellence in Basic Research in AIDS	1988
	Research Committee, American Cancer Society,	
	Illinois Division	1988-93
	Judge, Chicago Area Science Fair	1988-
	Convenor of the Hepatitis B Virus Workshop	
	Annual American Society for Virology Meeting	1990-92
	Member of a National Cancer Institute Review	
	Committee: Program Project Site Visits	1991,92
	Founding Member, Steering Committee, Chicago	·
	Area Virology Association	1992-95
	Ad hoc Member/Reviewer Reserve	
	Experimental Virology Study Section, NIAID, NIH	1993,95,96
	Ad hoc Member of the Virology Study Section, NIH	1993
	Member, National Board of Medical Examiners	
	Microbiology Test Committee, and United States	
*****	Medical Licensing Examination Step 1 Material	
	Development Committe for Microbiology	1994-97
	Ad hoc grant reviews for the National Institutes of Health,	
	National Science Foundation, Veteran's Administration,	
	U.S. Department of Agriculture, and Illinois Cancer Council	
	Ad hoc manuscript reviews for the Journal of	
	Virology, Journal of General Virology, Virus Research	
	and Viral Immunology	
PROFESSIONAL	American Society for Virology	
	can Society for Microbiology	
	American Association for the Advancement of Science	
	Society for General Microbiology	
	Sigma Xi: Secretary, Rush University Club	1986-88
	• • • • • • • • • • • • • • • • • • •	

EXTERNAL RESEARCH

Igen, Inc.

07/01/84 - 12/30/84

\$22,650

SUPPORT:

Principal Investigator: Mark E. Peeples, Ph.D.

"Pseudotype Virus Containing the Hepatitis B Glycoprotein: Development and Use"

National Institutes of Health (RO1 AI 21924)

07/01/85 - 06/30/88

\$235,405 Direct Costs

Principal Investigator: Mark E. Peeples, Ph.D.

"Structural/Functional Mapping of the NDV Matrix Protein"

American Cancer Society, Illinois Division (#85-47)

10/15/85 - 01/14/87

\$35,000

Principal Investigator: Mark E. Peeples, Ph.D.

"A Receptor for Hepatitis B Virus on Cultured Cells"

American Cancer Society, Illinois Division (#87-10)

01/15/87 - 03/14/88

\$35,000

Principal Investigator: Mark E. Peeples, Ph.D.

"Identification of the Hepatitis B Virus Receptor on Cultured Cells"

National Institutes of Health (RO1 AI 25586)

07/01/88 - 06/30/93

\$332,007 Direct Costs

Principal Investigator: Mark E. Peeples, Ph.D.

"Identification of a Cell Receptor for Hepatitis B Virus"

National Institues of Health (KO4 AI 00908)

07/01/88 - 06/30/93

\$234,000 Direct Costs

Research Career Development Award

Principal Investigator: Mark E. Peeples, Ph.D.

"Identification of a Cell Receptor for Hepatitis B Virus"

National Institutes of Health (RO1 AI 29606)

04/01/90 - 03/31/95

\$450,033 Direct Costs

Principal Investigator: Mark E. Peeples, Ph.D. Co-Principal Investigator: Kailash C. Gupta, Ph.D.

"NDV M Protein: Virion Assembly and Nuclear Location"

Analytab Products Incorporated, Diamedix

07/01/89 - 06/30/90

\$12,500

Principal Investigators: Mark Peeples, Ph.D., Jeffry Nelson, M.D.,

and Matthew Bankowski, Ph.D.

"Western Blot in the Diagnosis of Lyme Disease"

Cytel Corporation

09/01/90 - 08/31/91

\$50,000

Principal Investigator: Mark E. Peeples, Ph.D.

"The Hepatitis B Virus Receptor as an Antiviral Agent"

National Science Foundation 02/01/93-07/1/96

\$10,950

Principal Investigator: Mark E. Peeples, Ph.D.

Co-Principal Investigator: Jeffrey J. Gorman, Ph.D.

"U.S. Australia Cooperative Research: Interactions between the Two

Polypeptides of the Paramyxovirus Fusion Proteins"

National Institutes of Health (Continuation of RO1 AI 25586)

9/01/95 - 8/31/98

\$452,055 Direct Costs

Principal Investigator: Mark E. Peeples, Ph.D.

"Identification of a Cell Receptor for Hepatitis B Virus"

INVITED PRESENTATIONS AT OTHER INSTITUTIONS:

- 1. Evidence for a Hepatitis B Virus Receptor. Merck Sharpe & Dohme Research Laboratories, West Point, PA, October, 1986.
- 2. Is There More Than One Receptor for Hepatitis B Virus? Abbott Laboratories, Abbott Park, IL, July, 1987.
- 3. Does Hepatitis B Virus Have Two Receptors? Department of Immunology and Microbiology, Wayne State University School of Medicine, Detroit, MI, April, 1988.
- 4. The Paramyxovirus Matrix Protein: Assembly Band Leader and Nucleolar Groupie. Department of Biological Chemistry and Structure, The Chicago Medical School, North Chicago, IL, May, 1989.
- 5. The Paramyxovirus Matrix Protein: Band Leader of Assembly and Nucleolar Groupie. Department of Microbiology and Immunology, Indiana University School of Medicine, Indianapolis, IN, May, 1989.
- 6. Hepatitis B Virus: Is One Receptor Enough? Department of Microbiology and Immunology, University of Illinois at Chicago College of Medicine, March, 1990.
- 7. Hepatitis B Virus: Evidence for Two Receptors. Cytel Corporation, La Jolla, CA, March, 1990.
- 8. A Novel Receptor for Hepatitis B Virus. Department of Microbiology-Immunology, Northwestern Medical School, Chicago, IL, March, 1990.
- 9. Hepatitis B Virus: Would You Pick Up This Hitchhiker? Biology Department, Purdue University, Calumet, IN, March, 1990.
- 10. Hepatitis B Virus May Be a Hitchhiker. Department of Medical Microbiology, University of Alberta, Edmonton, Alberta, Canada, June, 1990.
- 11. The Hepatitis B Virus Receptor for Hepatocytes May Be a Lipoprotein, Heidelberg University, Heidelberg, Germany, September, 1990.
- 12. Hepatitis B Virus Receptor: An Apolipoprotein Hitchhiker? Department of Microbiology and Immunology, Loyola University, Strich School of Medicine, Maywood, IL, October, 1990.
- 13. A Hepatitis B Virus Binding Protein: Is It the Receptor? Biology Department, Purdue University, Calumet, IN, April, 1991.
- 14. The Paramyxovirus Fusion Glycoprotein, menage a deux au trois? Chicago Medical School, North Chicago, IL, March, 1992.

- 15. The Paramyxovirus Fusion Protein: Menage a deux au trois? University of Massachusetts Medical Center, Worcester, Mass., May, 1992.
- 16. Molecular Biology of Newcastle Disease Virus. Kalamazoo College, Kalamazoo, Michigan, October, 1992.
- 17. Signals Controlling Nuclear Localization of the Newcastle Disease Virus Matrix Protein. Biomolecular Research Institute, Parkville, Victoria, Australia, February, 1993.
- 18. Virus Attachment and Entry: Paramyxoviruses and Hepadnaviuses. Northern Illinois University, DeKalb, Illinois, February, 1994.
- 19. How to Identify a Virus Receptor. Pro-Virus Incorporated, Rockville, Maryland, March, 1995.
- 20. Hepatitis Viruses. Associated Colleges of the Chicago Area, Argonne National Laboratory, Illinois, April, 1995.
- In Search of the Hepatitis B Virus Receptor. Biology Department, Purdue University, Calumet, IN, April, 1995.
- 22. Apolipoprotein H: Potential Hepatitis B Virus Receptor. Biomolecular Research Institute, Melbourne, Australia. October, 1995.

PUBLICATIONS:

- 1. Levine, S., Peeples, M. and Hamilton, R. 1977. The effect of respiratory syncytial virus infection on HeLa-cell macromolecular synthesis. J. Gen. Virol., 37:53-63.
- 2. Peeples, M.E. 1978. Studies on the polypeptide structure, the metabolic requirements for maturation, and persistence of respiratory syncytial (RS) virus in HeLa cell culture: Doctoral Dissertation.
- 3. Peeples, M. and Levine, S. 1979. Respiratory syncytial virus polypeptides: their location in the virion. Virology <u>95</u>:137-145.
- 4. Peeples, M. and Levine, S. 1980. Metabolic requirements for the maturation of respiratory syncytial (RS) virus. J. Gen. Virol. <u>50</u>:81-88.
- 5. Peeples, M.E. and Levine, S. 1981. Characteristics of a persistent respiratory syncytial virus infection in HeLa cells. Virology 113:141-149.
- 6. Peeples, M.E. and Bratt, M.A. 1982. UV irradiation analysis of complementation between, and replication of, RNA-negative temperature-sensitive mutants of Newcastle disease virus. J. Virol. 41:965-973.
- 7. Peeples, M.E. and Bratt, M.A. 1982. Virion functions of RNA⁺ temperature-sensitive mutants of Newcastle disease virus. J. Virol. 42:440-446.
- 8. Peeples, M.E., Rasenas, L.L. and Bratt, M.A. 1982. RNA synthesis by Newcastle disease virus temperature-sensitive mutants in two RNA-negative complementation groups. J. Virol. 42:996-1006.
- 9. Peeples, M.E., Glickman, R.L. and Bratt, M.A. 1983. Thermostabilities of virion activities of Newcastle disease virus: evidence that the temperature-sensitive mutants in groups B, BC, and C have altered HN proteins. J. Virol. 45:18-26.
- 10. Peeples, M.E. and Bratt, M.A. 1984. Mutation in the matrix protein of Newcastle disease virus can result in decreased fusion glycoprotein incorporated into virion particles and decreased infectivity. J. Virol. <u>51</u>:81-90.

- 11. Morrison, T.G., Peeples, M.E. and McGinnes, L.W. 1987. Conformational change in a viral glycoprotein during maturation due to disulfide bond disruption. Proc. Natl. Acad. Sci., U.S.A. 84:1020-1024.
- 12. Peeples, M.E., Komai, K., Radek, R. and Bankowski, M.J. 1987. A cultured cell receptor for the small S protein of hepatitis B virus. Virology 160:135-142.
- 13. Faaberg, K.S. and Peeples, M.E. 1988. Strain variation and nuclear location of the Newcastle disease virus matrix protein. J. Virol. <u>62</u>:586-593.
- 14. Peeples, M.E. 1988. Differential detergent treatment allows immunofluorescent localization of the matrix protein of Newcastle disease virus within the nucleus of infected cells. Virology 162:255-259.
- 15. Komai, K., Kaplan, M. and Peeples, M.E. 1988. The Vero cell receptor for the hepatitis B virus small S protein is a sialoglycoprotein. Virology <u>163</u>:629-634.
- 16. Peeples, M.E., Glickman, R.L., Gallagher, J.P. and Bratt, M.A. 1988. Temperature-sensitive mutants of Newcastle disease virus altered in HN glycoprotein size, stability, or antigenic maturity. Virology 164:284-289.
- 17. Faaberg, K.S. and Peeples, M.E. 1988. Association of the soluble matrix protein of Newcastle disease virus with liposomes is independent of ionic conditions. Virology 166:123-132.
- 18. Pontisso, P., Petit, M.-A., Bankowski, M.J. and Peeples, M.E. 1989. Human liver membranes contain receptors for the hepatitis B virus pre-S1 region and, via polymerized human serum albumin, for the pre-S2 region. J. Virol. 63:1981-1988.
- 19. Niles, W.D., Peeples, M.E. and Cohen, F.S. 1990. Kinetics of virus-induced hemolysis measured for single erythrocytes. Virology 174:593-598.
- 20. Nelson, J.A., Bankowski, M.J., Newton, B.J., Benson, C.A., Kaplan, R., Landau, W., Trenholme, G.M. and Peeples, M.E. 1990. Detection of antibodies in late lyme disease. J. Infect. Dis. 161:1034-1035.
- 21. Komai, K. and Peeples, M.E. 1990. Hepatitis B virus surface antigen particles are internalized by Vero cells. Virology <u>177</u>:332-338.
- Nelson, J.A., Bouseman, J.K., Kitron, U., Callister, S.M., Harrison, B., Bankowski, M.J.,
 Peeples, M.E., Newton, B.J. and Anderson, J.F. 1991. Isolation and characterization of <u>Borrelia burgdorferi</u> from Illinois <u>Ixodes dammini</u>. J. Clin. Microbiol. <u>29</u>:1732-1734.
- 23. Mehdi, H., Nunn, M., Steel, D.M., Whitehead, A.S., Perez, M., Walker, L. and Peeples, M.E. 1991. Nucleotide sequence and expression of the human gene encoding apolipoprotein H (B2-glycoprotein I). Gene 108:293-298.
- Nelson, J.A., Wolf, M.D., Yuh, W.T.C. and Peeples, M.E. 1992. Cranial nerve involvement with Lyme borreliosis demonstrated by magnetic resonance imaging. Neurology 42:671-673.
- 25. Peeples, M.E., Wang, C., Gupta, K.C. and Coleman, N. 1992. Nuclear entry and nucleolar localization of the Newcastle disease virus (NDV) matrix protein occurs early in infection and does not require other NDV proteins. J. Virol. 66:3263-3269.
- Wang, C., Raghu, G., Morrison, T. Peeples, M.E. 1992. Intracellular processing of the paramyxovirus F protein: critical role of the predicted amphipathic alpha helix adjacent to the fusion domain. J. Virol. 66:4161-4169.
- 27. Reichard, K.W., Lorence, R.M., Cascino, C.J., Peeples, M.E., Walter, R.J., Fernando, M.B., Reyes, H.M. and Greager, J.A. 1992. Newcastle disease virus selectively kills human tumor cells. J. Surg. Res. <u>52</u>:448-453.
- Wolf, M.D., Folk, J.C., Nelson, J.A. and Peeples, M.E. 1992. Acute posterior multifocal placoid pigment epitheliopathy and Lyme disease. (Correspondence) Arch. Ophthalmol. 110:750.

- 29. Sergel, T., McGinnes, L.W., Peeples, M.E. and Morrison, T.G. 1993. The attachment function of the Newcastle disease virus hemagglutinin-neuraminidase protein can be separated from fusion promotion by mutation. Virology 193:717-726.
- Reichard, K.W., Katubig, B.B., Reyes, H.M., Peeples, M.E. and Lorence, R.M. 1993. Retinoic acid enhances killing of neuroblastoma cells by Newcastle disease virus. J. Ped. Surg. 28:1221-1226.
- 31. Coleman, N. and Peeples, M.E. 1993. The matrix protein of Newcastle disease virus localizes to the nucleus via a bipartite nuclear localization signal. Virology 195:596-607.
- 32. Anderson, K.M., Peeples, M.E. Kessler, H., and Harris, J.E. 1993. Neither ETYA nor A63162 inhibit Newcastle disease, herpes simplex or simian virus 40 replication: implications for their mechanism of action. Clin. Physiol. Biochem. 10:65-70.
- 33. Melikyan, G.B., Niles, W.D., Peeples, M.E. and Cohen, F.S. 1993. Influenza hemagglutinin-mediated fusion pores connecting cells to planar membranes: flickering to final expansion. J. Gen. Physiol. 102:1131-1149.
- 34. Sellar, G.C., Keane, J., Mehdi, H., Peeples, M.E., Browne, N. and Whitehead, A.S. 1993. Characterization and acute phase modulation of canine apolipoprotein H (β2-glycoprotein I). Biochem. Biophys. Res. Comm. 191:1288-1293.
- 35. Mehdi, H., Kaplan, M.J., Anlar, F.Y., Yang, X., Bayer, R., Sutherland, K., and Peeples, M.E. 1994. Hepatitis B virus surface antigen binds to apolipoprotein H. J. Virol. <u>68</u>:2415-2424.
- 36. Lorence, R.M., Reichard, K.W., Katubig, B.B., Reyes, H.M., Phuangsab, A., Mitchell, B.R., Cascino, C.J., Walter, R.J., and Peeples, M.E. 1994. Complete regression of human neuroblastoma xenografts in athymic mice after local Newcastle disease virus therapy. J. Natl. Cancer Inst. 86:1228-1233. [Accompanying editorial: Kenney, S. and Pagano, J., Viruses as oncolytic agents: a new age for "therapeutic" viruses? J. Natl. Cancer Inst. 86:1185-1186.]
- 37. Lorence, R.M., Katubig, B.B., Reichard, K.W., Reyes, H.M., Phuangsab, A., Sassetti, M.D., Walter, R. J., and Peeples, M.E. 1994. Complete regression of human fibrosarcoma xenografts after local Newcastle disease virus therapy. Cancer Research 54:6017-6021.
- 38. Wang, C. and Peeples, M.E. 1995. Intracellular maturation of the Newcastle disease virus fusion protein is affected by strain differences in the predicted amphipathic α-helix adjacent to the fusion domain. Virology 208:827-831.
- 39. Saifuddin, M., Parker, C.J., Peeples, M.P., Gorney, M.K., Zolla-Pazner, S., Ghassemi, M., Rooney, I.A., Atkinson, J.P., Spear, G.T. 1995. Role of virion-associated glycosylphosphatidyl-inositol-linked proteins CD55 and CD59 in complement resistance of cell line-derived and primary isolates of HIV-1. J. Exper. Med., 182:501-509.
- 40. Mehdi, H., Yang, X., and Peeples, M.E. 1996. An altered form of apolipoprotein H binds hepatitis B surface antigen most efficiently. Virology 217:58-66.

MANUSCRIPTS IN PREPARATION:

- 1. Lorence, R.M., Katubig, B.B., Sassatti, M.D., Reyes, H.M., Phuangsab, A., Reichard, K.W., Peeples, M.E., and Walter, R. J. Growth inhibition of human colon and prostate adenocarcinoma and epidermoid carcinoma xenografts after local Newcastle disease virus therapy.
- 2. Coleman, N. and Peeples, M.E. Identification of a region of the Newcastle disease virus matrix protein required for cytoplasmic localization.

3. Peeples, M.E., Newton, B., Raghu, G., Robey, F., Bencsics, C. and Wang, C. Oligomeric forms of the Newcastle disease virus fusion glycoprotein and determinants of their structure.

BOOK CHAPTERS:

- 1. Peeples, M.E., Gallagher, J.P. and Bratt, M.A. 1981. Permissive temperature analysis of RNA⁺ temperature-sensitive mutants of Newcastle disease virus, p. 567-572 in "The Replication of Negative Strand Viruses," D.H.L. Bishop and R.W. Compans, eds. Elsevier North Holland, Inc., New York.
- 2. Peeples, M.E. and Bratt, M.A. 1984. Mapping mutant and wild-type M proteins of Newcastle disease virus (NDV) by repeated partial proteolysis, p. 315-320. In Nonsegmented Negative Strand Viruses, D.H.L. Bishop and R.W. Compans, eds., Academic Press, New York.
- 3. Peeples, M.E. 1987. A ts mutant of Newcastle disease virus that is defective in F_o cleavage and antibody binding under nonpermissive conditions, p. 81-88, In B.W.J. Mahy and D. Kolakofsky (ed). The Biology of Negative Strand Viruses, Elsevier Biomedical Press, New York.
- 4. Pontisso, P., Bankowski, M.J., Petit, M.-A. and Peeples, M.E. 1987. Recombinant HBsAg particles containing pre-S proteins bind to human liver plasma membranes, p. 205-221, In W. Robinson, K. Koike and H. Will (ed.) <u>Hepadna Viruses</u>, Alan R. Liss, Inc., New York.
- 5. Reichard, K.W., Lorence, R.M., Casino, C.J., Peeples, M.E., Walter, R.J., and Reyes, H.M. 1992. N-myc oncogene enhances the sensitivity of neuroblastoma to killing by Newcastle disease virus, p. 603-606, In Mason, S.K. and Oliver, K.C. (ed.) Surgical Forum, Volume XLIII, American College of Surgeons, Chicago, IL.

INVITED REVIEWS:

- 1. Peeples, M.E. Newcastle disease virus replication, In D.J. Alexander (ed.) <u>Newcastle Disease</u>, p. 45-78. Kluwer Academic Publishers, Boston, MA, 1988.
- 2. Peeples, M.E. Paramyxovirus M proteins: Pulling it all together and taking it on the road, p. 427-456, In D.W. Kingsbury (ed.) The Paramyxoviruses, Plenum Press, New York, NY, 1991.
- 3. Peeples, M.E. The hepatitis B virus receptor: Book 'em, Dano?, In T.J. Liang (ed.) "Elsewhere" section, Hepatology, 20:1364-1366, 1994.

SCIENTIFIC WRITING FOR THE GENERAL PUBLIC:

1. Peeples, M.E. Huntington's Handle, In Stanley Schmidt (ed.) <u>Analog Science Fiction/Science Fact</u>, p. 72-84. Davis Publications, Inc., New York, NY, October, 1987. Reprinted In Stanley Schmidt (ed.) <u>Analog Essays on Science</u>, p. 179-192. John Wiley and Sons, Inc., New York, NY, 1990.

ABSTRACTS AND MEETING PRESENTATIONS:

1. Peeples, M. and Levine, S. System for studying late metabolic events in respiratory syncytial (RS) virus synthesis. Abstr. Annu. Mtg. Amer. Soc. Microbiol. 1976.

- 2. Peeples, M. and Levine, S. Effect of respiratory syncytial (RS) virus on HeLa cell synthesis. Abstr. Annu. Mtg. Amer. Soc. Microbiol. 1977.
- 3. Peeples, M. and Levine, S. Effects of trypsin on cell-associated respiratory syncytial (RS) virus. Abstr. Annu. Mtg. Amer. Soc. Microbiol. 1978.
- 4. Peeples, M.E., Kotilainen, H.R., Rasenas, L.L., Gallagher, J.P. and Bratt, M.A. Complementation studies of Newcastle disease virus (NDV) ts mutants and preliminary characterization of the two RNA groups, A and E. Abstr. in J. Supramol. Struct., Suppl. 4, 1980.
- 5. Peeples, M.E. and Bratt, M.A. UV-irradiation analysis of Newcastle disease virus (NDV) tsRNA mutant complementation. Fifth International Congress of Virology, Abstracts. 1981.
- 6. Peeples, M.E. and Bratt, M.A. Is the M protein of Newcastle Disease Virus involved in hemolysis and infectivity? Annu. Mtg. Amer. Soc. Virol. 1982.
- 7. Peeples, M.E. and Bratt, M.A. Mapping the M protein of Newcastle Disease Virus by repeated partial proteolysis and subsequent location of an alteration in a ts mutant. Annu. Mtg. Amer. Soc. Virol. 1983.
- 8. Faaberg, K. and Peeples, M. Newcastle disease virus matrix protein associates with liposomes of positive, negative, and neutral charge. Sixth International Congress of Virology, P12-2, p.358, 1984.
- 9. Peeples, M.E. A ts mutant of Newcastle disease virus that is defective in F_o cleavage and in antibody binding under nonpermissive conditions. Sixth International Meeting on Negative Strand Viruses. Virus Research, Supplement 1:29, 1985.
- 10. Morrison, T.G., Peeples, M., McGinnes, L. Conformational changes in the NDV fusion protein detected by monoclonal antibodies. Annu. Mtg. Amer. Soc. Virol. June 1986.
- 11. Faaberg, K., Peeples, M. Monoclonal antibodies define three strain-variable epitopes on the NDV M protein. Annu. Mtg. Amer. Soc. Virol. June 1986.
- 12. Peeples, M., Radek, R., Komai, K. A cultured cell line expressing a receptor for hepatitis B virus surface antigen. Annu. Mtg. Soc. Virol. June 1986.
- 13. Peeples, M. NDV M protein in the nucleus of infected cells. Annu. Mtg. Amer. Soc. Virol. June 1986.
- 14. Peeples, M.E., Komai, K., Radek, R., Bankowski, M.J. A cultured cell line expressing a functional receptor for hepatitis B surface antigen. Cold Spring Harbor Meeting, Molecular Biology of Hepatitis B Viruses. Abstracts, p. 76. 1986.
- Pontisso, P., Bankowski, M., Peeples, M. Evidence for hepatitis B virus middle S protein binding to human liver membranes. UCLA Symposium on Hepadna Viruses Molecular Biology, J. of Cell. Biochem., Supplement 11D, p. 19, Abstract 0113. 1987.
- 16. Pontisso, P., Peeples, M., Bankowski, M. Middle S protein containing HBsAg particles bind to liver cell membranes in the presence of polyalbumin. International Symposium on Viral Hepatitis and Liver Disease. J. Med. Virol. 21(4), p. 56A, Abstract 160. 1987.
- 17. Faaberg, K.S. and Peeples, M.E. Monoclonal antibodies reveal a specific association between the M protein of Newcastle disease virus and liposomes. VII International Congress of Virology, p. 272, Abstract OP10.1. 1987.
- 18. Komai, K. and Peeples, M.E. The Vero cell receptor for hepatitis B virus small S protein is a sialoglycoprotein. VII International Congress of Virology, p. 142, Abstract R17.19. 1987.
- 19. Bankowski, M.J., Ogston, C.W., Pontisso, P., Komai, K. and Peeples, M.E. Attachment of DNA-containing hepatitis B virus particles to a monkey kidney cell line. VII International Congress of Virology, p. 142, Abstract R17.20. 1987.

- 20. Pontisso, P., Petit, M.-A., Bankowski, M. and Peeples, M. Normal human liver plasma membranes bear two distinct receptors for hepatitis B virus: one for pre-S1 and another for pre-S2. Cold Spring Harbor Meeting, Molecular Biology of Hepatitis B Viruses. Abstracts, p. 59.
- 21. Pontisso, P., Ogston, C.W. and Peeples, M.E. <u>In vitro</u> binding of hepatitis B virus surface proteins to human leukocytes. Cold Spring Harbor Meeting, Molecular Biology of Hepatitis B Viruses. Abstracts, p. 63. 1987.
- 22. Pontisso, P., Bankowski, M., Alberti, A. and Peeples, M.E. Recombinant HBsAg particles binding to human liver membranes. 20^a Riunione Generale Annuale. Association Italiana Per Lo Studio Del Fegato. Abstracts, p. 4. 1987.
- 23. Pontisso, P., Bankowski, M.J., Petit, M.A., Alberti, A. and Peeples, M.E. Two distinct receptors on normal human liver plasma membranes bind pre-S1 and pre-S2 encoded proteins. 22nd Meeting of the European Association for the Study of the Liver. J. Hepatol., Suppl. 1, p. S52, Abstract 92, 1987.
- 24. Bankowski, M., Kaplan, M. and Peeples, M. Cultured human hepatoma cells express a receptor activity for hepatitis B virus large S protein. Molecular Biology of Hepatitis B Viruses Meeting, Abstracts, p. 53, 1988.
- 25. Peeples, M. The Newcastle disease virus fusion glycoprotein is a noncovalent multimer which is disrupted and loses antigenicity upon boiling. 7th International Meeting on Negative Strand Viruses. Virus Res., Suppl. 2, p. 15, Abstract 28, 1988.
- 26. Niles, W.D., Peeples, M.E. and Cohen, F.S. A model system for virus-membrane interactions. J. Cell Biol. 107:103a, 1988.
- Niles, W.D., Peeples, M.E., Cohen, F.S. Video microscopy studies of virus-membrane interactions. Biophys. J. 55:602a, 1989.
- 28. Peeples, M.E. and Bencsics, C. Oligomeric structure of the Newcastle disease virus F glycoprotein. Annual Meeting of the American Society for Virology, London, Ontario, 1989.
- 29. Coleman-Fuller, N., Gupta, K.C., Patwardhan, S. and Peeples, M.E. Newcastle disease virus M protein does not require other viral proteins for nuclear transport. Annual Meeting of the American Society for Virology, London, Ontario, 1989.
- 30. Kaplan, M. and Peeples, M. Candidate receptors for hepatitis B virus on a human hepatoma cells line. Annual Meeting of the American Society for Virology, London, Ontario, 1989.
- Kaplan, M. and Peeples, M. Receptor candidates for the hepatitis B virus on the HepG2 human hepatoma cell line. Meeting on Hepatitis B Viruses, Abstracts, p. 95, 1989.
- 32. Glinski, B.M., Bankowski, M.J., Newton, B.J., Miller, K. and Peeples, M.E. Antibodies to Borrelia burgdorferi in Canine Serum: Western Blot. Annual Meeting of the American Society for Microbiology, Abstract C116, p. 363, 1990.
- 33. Peeples, M.E., Anlar, F.Y. and Kaplan, M.J. An apolipoprotein heterodimer binds specifically to the hepatitis B virus large S protein. Annual Meeting of the AMerican Society for Virology, University of Utah, Salt Lake City, 1990.
- Wang, C. Ganapathirama, R. and Peeples, M. The three group D ts mutants of Newcastle disease virus contain F gene lesions. American Society for Virology 9th Annual Meeting, University of Utah, Salt Lake City, Utah, 1990.
- 35. Kaplan, M.J., Anlar, F.Y. and Peeples, M.E. A 46kDa lipoprotein which binds hepatitis B virus large S protein. Molecular Biology of Hepatitis B Viruses, University of California, San Diego, Abstracts, p. 82, 1990.
- 36. Kaplan, M.J., Anlar, F. and Peeples, M.E. The hepatitis B virus receptor may be an apolipoprotein. VIIIth International Congress of Virology, Berlin, Abstract W10-6, 1990.

- 37. Glinski, B.M., Schillhorn van Veen, T.W., Murphy, A.J., Harrison, B., Newton, B. and Peeples, M.E. Detection of Antibodies to <u>Borrelia burgdorferi</u> in Canine Sera: A Comparison Study. American Society for Microbiology, Dallas, Texas, p. 394, Abstract #C316, 1991.
- 38. Anlar, F.Y., Yang, X., Kaplan, M.J. and Peeples, M.E. Recombinant hepatitis B virus large surface protein binds to apolipoprotein H. Annual Meeting of the American Society for Virology, Colorado State University, Ft. Collins, CO, July, 1991.
- 39. Mehdi, H., Nunn, M., Walker, L., Perez, M., Whitehead, A. and Peeples, M. Sequence and expression of an HBsAg binding protein apolipoprotein H. Annual Meeting of the American Society for Virology, Colorado State University, Ft. Collins, CO, 1991.
- 40. Coleman-Fuller, N. and Peeples, M.E. Identification of a nuclear exit signal in the matrix protein of Newcastle disease virus strain HP. American Society for Virology 10th Annual Meeting, Colorado State University, Fort Collins, CO, 1991.
- 41. Wang, C., Raghu, G. and Peeples, M.E. Localization of two Newcastle disease virus ts lesions to a heptad repeat in the F glycoprotein. Negative Strand Viruses 8th International Conference, Charleston, SC, Abstract #18, 1991.
- 42. Coleman-Fuller, N. and Peeples, M.E. The matrix protein of Newcastle disease virus contains a multi-component nuclear localization signal. Negative Strand Viruses 8th International Conference, Charleston, SC, Abstract #81, 1991.
- 43. Mehdi, H., Nunn, M., Walker, L., Perez, M., Whitehead, A. and Peeples, M.E. Cloning and transient expression of apolipoprotein H, an HBsAg binding protein. Molecular Biology of Hepatitis B viruses, Paris, France, Abstract #43, 1991.
- 44. Lorence, R.M., Riechard, K.W., Casino, C.J. and Peeples, M.E. Ras-transformation of human fibroblasts enhances cytotoxicity and replication by Newcastle disease virus (NDV). Proceedings, Eighty-Third Annual Meeting of the American Association Of Cancer Research, San Diego, CA, Volume 33, Abstract #2378, 1992.
- 45. Reichard, K.W., Lorence, R.M., Casino, C.J., Peeples, M.E., Reyes, H.M. and Greager, J.A. Selective replication of Newcastle disease virus (NDV) in cancer cells is associated with virus-induced cell fusion. Proceedings, Eighty-Third Annual Meeting of the American Association for Cancer Research, San Diego CA. Volume 33, Abstract #3116, 1992.
- Anderson, K.M., Peeples, M., Kessler, H., and Harris, J.E. ETYA (5,8,11,14-eicosatetraynoic acid) does not inhibit Newcastle disease virus or herpes simplex virus replication. Proceedings, Eighty-Third Annual Meeting of the American Association for Cancer Research, San Diego, CA. Volume 33, Abstract #3058, 1992.
- 47. Harrison, B., Bankowski, M.J., Wood, N.B., Kerns, L., Trenholme, Benson, C., Peeples, M.E. and Landay, A. Detection of herpes simplex virus polymerase chain reaction (PCR) product using digoxygenin-labeled, PCR-produced probe. American Society for Microbiology Annual Meeting, New Orleans, LA. Abstract #C163. 1992.
- 48. Yang, X., Mehdi, H. and Peeples, M.E. Recombinant HBsAg particles containing the small S protein of hepatitis B virus specifically bind to apolipoprotein H. American Society for Virology Annual Meeting, Cornell University, Ithaca, N.Y., July, 1992.
- Wang, C., Taylor, S. and Peeples, M.E. The F protein of Newcastle disease virus, strain AV, is ts in intracellular processing: Role of the amphipathic alpha helix adjacent to the fusion domain. American Society for Virology Annual Meeting, Cornell University, Ithaca, N.Y., July, 1992.
- Yang, X., Mehdi, H. and Peeples, M.E. Specific binding of recombinant HBsAg particles to apolipoprotein H. Molecular Biology of Hepatitis B Viruses Meeting, University of California, San Diego, August, 1992. Abstract #57.

- 51. Wang, C. and Peeples, M.E. Proper disulfide bond formation in the fusion protein of Newcastle disease virus depends on an intact α helix. Lorne Conference on Protein Structure and Function, Lorne, Victoria, Australia, Abstract #23, 1993.
- 52. Lorence, R.M., Peeples, M.E., Katubig, B.B., Reichard, K.W., daSilva, A.F., Phuangsab, A., Mitchell, B.R., Walter, R.J., and Reyes, H.M. Complete regression of human fribrosarcoma xenografts after local treatment with Newcastle disease virus. American Society for Virology Annual Meeting, University of California, Davis, July, 1993. Abstract #44-9.
- 53. Taylor, S.S. and Peeples, M.E. Newcastle disease virus fusion protein is homooligomeric. American Society for Virology Annual Meeting, University of California, Davis, July, 1993. Abstract #44-10.
- 54. Nelson, J.A., Peterson, K., Newton, B.J., Harrison, B., Picken, R.N., and Peeples, M.E. Demonstration of the heterogeneous nature of *Borrelia burgdorferi* from Illinois. ICAAC Annual Meeting, New Orleans, 1993. Abstract #1611, p.413.
- 55. Pratuangtham, S. and Peeples, M.E. Polyethylene glycol enhances hepatitis B virus binding to, and infection of primary hepatocytes. American Society for Virology Annual Meeting, University of Wisconsin, Madison, July, 1994, Abstract #42-8, p.253.
- 56. Lorence, R.M., Reichard, K.W., Reyes, H.M., Katubig, B.B., Phuangsab, A., Walter, R.J., Rojas, R.A., da Silva, A.F., Ringwald, J., and Peeples, M.E. Regression of Human Tumor xenografts in athymic mice after treatment with Newcastle disease virus. American Society for Virology Annual Meeting, University of Wisconsin, Madison, July, 1994, Abstract #W23-4, p.190.
- 57. Coleman, N. and Peeples, M.E. A signal in the matrix protein of one strain of Newcastle disease virus that causes cytoplasmic localization late in infection. Ninth International Conference on Negative Strand Viruses, Estoril, Portugal, October, 1994, Abstract #14, p.49.
- 58. Siddiqi, A., Peeples, M., Brees, A., Moy, J. Respiratory syncytial virus-induced release of RANTES and MIP-1a by broncial epithelial and peripheral mononuclear cells. 51st Annual Meeting of the American Academy of Allergy and Immunology, February, 1995. J. Allergy Clin. Immunology 97:305, 1996.
- 59. Peeples, M.E., and Collins, P.L. The 4C mutation that enhances respiratory syncytial virus minigenome replication enhances encapsidation rather than promotor activity. 15th Annual Meeting of the American Society for Virology, University of Western Ontario, July, 1996. Abstract W37-5, p. 148.

GRADUATE STUDENT ADVISEES:

- Kay S. Faaberg. Antigenic Mapping and Model Membrane Association of the Newcastle Disease Virus Matrix Protein. 1982-1987, Ph.D.
- Matthew J. Bankowski. The Envelope Proteins of Hepatitis B Virus: Evidence for a New Protein and Identification of a Viral Attachment Protein. 1982-1988, Ph.D.
- Michael J. Kaplan. A Candidate Receptor for Hepatitis B Virus. 1985-1991, Ph.D.
- Natalie Coleman. Nuclear Localization of the Newcastle Disease Virus Matrix Protein. 1988-1992,
- Can Wang. Genetic Analysis of the Newcastle Disease Virus Fusion Protein. 1987-93, Ph.D.
- Karen Sutherland. Association Between Hepatitis B Virus and Apolipoprotein H in Chronically Infected Patients. 1988-

- Lisa Scott. Identification of the Respiratory Syncytial Virus Receptor. 1991-
- Edgardo Ariztia. Hepatocyte Growth Factor-Induced Gene Expression in Liver Epithelial Cells. (Co-Advisor with Anand Iyer, Northwestern Medical College) 1992-
- Louay Hallak. Ribozyme against Hepatitis B Virus. 1994-

POSTDOCTORAL TRAINEES/VISITING SCIENTISTS/RESIDENTS:

- Kazuo Komai, M.D. The Vero Cell Receptor for Hepatitis B Virus Small Surface Protein. 1986.
- Patrizia Pontisso, M.D. Human Liver Plasma Membranes Contain a Binding Activity for the Hepatitis B Virus Large Surface Protein. 1986-1987.
- Ganapathirama Raghu, Ph.D. Sequence Analysis of the Newcastle Disease Virus Group D Temperature-Sensitive Mutants. 1986-88.
- Matthew J. Bankowski, Ph.D. Polymerase Chain Reaction Analysis of Human Immunodeficiency Virus Load in Patients Undergoing Drug Therapy. 1988-90.
- Fehim Yasar Anlar, M.D. Lipoprotein Association and Hepatitis B Virus Binding Activities of Apolipoprotein H. 1989-91.
- Yang Xu, M.D. Association of Serum-Derived Hepatitis B Virus Dane Particles with Apolipoprotein H. 1990-92.
- Haider Mehdi, Ph.D. Cloning, Sequencing and Expression of the Human Apolipoprotein H Gene. 1990-94.
- Robert Lorence, M.D., Ph.D. Newcastle Disease Virus Is Cytolytic to Tumor but not Normal Human Cells. 1990-95
- Mukul Rawat, Ph.D. Hepatitis B Virus Interactions with Serum Lipoproteins During Infection. 1991-93.
- Surasak Pratuangtham, M.D. Hepatitis B Virus Infection of Cultured Primary Human Hepatocytes. 1992-96.
- Ekkerhart Lausch, M.D. Hepatitis B Virus Receptor Identification. 1994-